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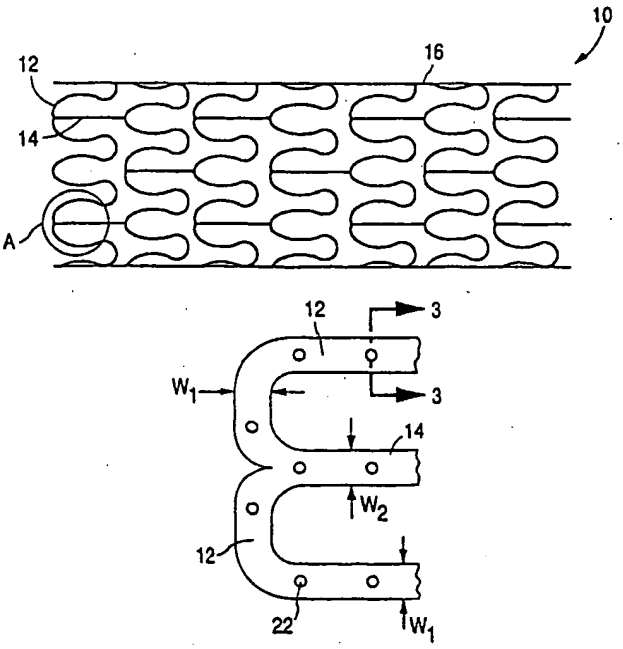
(54) Title: A POROUS PROSTHESIS AND A METHOD OF DEPOSITING SUBSTANCES INTO THE POROUS



(57) Abstract: An implantable prosthesis, for example a stent, is provided that is capable of being loaded with substances for subsequent application to biological tissues. In one example, the prosthesis is a cylindrical-shaped body having depots or pores formed thereon. The depots can be formed at preselected locations on the body of the prosthesis and can have a preselected depth, size, and shape. The deports can have various shapes including a cylindrical or a conical shape. Substances such as therapeutic substances, polymeric materials, polymeric materials containing therapeutic substances, radioactive isotopes, and radiopaque materials can be deposited into the depots. A method of loading a substance into the prosthesis having depots or pores is also provided. A first fluid in combination with an added substance is applied to the porous prosthesis. During the application, the first fluid containing the substance is capable of penetrating into prosthesis pores. The first fluid is removed and a second fluid is applied to the prosthesis.The second fluid is not capable of significantly penetrating into the pores. Prior to the application of the second fluid, the prosthesis can be immersed in a third fluid and agitated via mechanical perturbation techniques so that any of the substance gathered on the surface of the body, after the application of the first fluid, is removed. The third fluid should not be capable of dissolving the substance.

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A POROUS PROSTHESIS AND A METHOD OF DEPOSITING SUBSTANCES INTO THE PORES

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates to implantable devices, such as an expandable, intraluminal prosthesis commonly known as a stent. More particularly, this invention relates to a prosthesis having pores formed in its cylindrical body. Moreover, the present invention relates to a method of depositing substances, such as therapeutic substances, in the pores.

Description of the Background

Percutaneous transluminal coronary angioplasty (PTCA) is a procedure for treating heart disease. A catheter assembly having a balloon portion is introduced into the cardiovascular system of a patient via the brachial or femoral artery. The catheter assembly is advanced through the coronary vasculature until the balloon portion is positioned across the occlusive lesion. Once in position across the lesion, the balloon is inflated to a predetermined size to radially compress the atherosclerotic plaque of the lesion against the inner wall of the artery to dilate the lumen. The balloon is then deflated to a smaller profile to allow the catheter to be withdrawn from the patient's vasculature.

A problem associated with the procedure includes formation of intimal flaps or torn arterial linings which can collapse and occlude the conduit after the balloon is deflated. Moreover, thrombosis and restenosis of the artery may develop over several months after the procedure, which may require another angioplasty procedure or a surgical by-pass operation. To reduce the partial or

coated metallic stent, whereby a heparin coating is ionically or covalently bonded to the stent. Disadvantages associated with the aforementioned methods include significant loss of the therapeutic substance from the body of the stent during delivery and expansion of the stent and an absolute lack of control of the release rate of the therapeutic substance from the stent. Another proposed method involves the use of a polymeric carrier coated onto the body of the stent, as disclosed in U.S. Patent No. 5,464,650 issued to Berg et al., U.S. Patent No. 5,605,696 issued to Eury et al., U.S. Patent No. 5,865,814 issued to Tuch, and U.S. Patent No. 5,700,286 issued to Tartaglia et al. Obstacles often encountered with the use of a polymeric coating include difficulties in coating a complicated geometrical structure, poor adhesion of the polymeric coating to the surface of a stent, and biocompatibility of the polymer. Accordingly, it is desirable to be able to secure the therapeutic substance directly onto the body of the stent. Not withstanding the benefits gained by securing a therapeutic substance to the body of the stent, it is also desirable to be able to secure other substances to the body of the stent, such as radiopaque materials, used to assist a physician to guide and deploy the stent at the proper site of treatment.

SUMMARY OF THE INVENTION

In accordance with various aspects of the present invention, an implantable prosthesis, one example of which includes a stent, is provided that is capable of being loaded with substances. The prosthesis is defined by a cylindrical shaped body having a thickness. Depots or pores are formed on the body at preselected locations. The depots have a preselected depth and shape. The depth of the depots can be equal to about 10% to about 90% of the thickness. In one embodiment, the depots can have a cylindrical shape. In another embodiment, the shape can be generally conical. Substances such as therapeutic substances, polymeric material, polymeric material containing therapeutic substances, radioactive isotopes, and radiopaque material can be deposited into the depots.

Another aspect of the present invention is a method of loading a substance into the depots. The method is applicable not only to the above-described

Figure 2 is an enlarged view of section A of Figure 1, illustrating a portion of the cylindrical elements and connecting elements;

Figure 3A is a cross sectional view of the cylindrical element, taken in the direction of the arrows and along the plane of line 3-3 of Figure 2, illustrating a depot formed in the body of the prosthesis in accordance to one embodiment of the present invention;

Figure 3B is a cross sectional view of the cylindrical element, taken in the direction of the arrow and along the plane of line 3-3 of Figure 2, illustrating a depot formed in the body of the prosthesis in accordance to another embodiment of the present invention;

Figure 4A illustrates a fluid on a solid surface having a contact angle Φ_1; and

Figure 4B illustrates a fluid on a solid surface having a contact angle Φ_2.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Figure 1 illustrates an implantable prosthesis 10, one example of which includes a stent. Stents are scaffoldings, usually cylindrical or tubular in shape, that are inserted into a anatomical passageway and operate to physically hold open and, if desired, to expand the wall of a passageway. Stents are capable of being compressed for insertion through small cavities via balloon-catheters, positioned in a desired location, then expanded to a larger diameter.

In one example, illustrated in Figures 1 and 2, stent 10 includes a plurality of rigid but resiliently flexible thread elements 12 that are arranged in a sinusoid-like configuration that is connected to form a continuous ring or cylinder. The plurality of cylindrical thread elements 12 are radially expandable, disposed coaxially, and interconnected by connecting elements 14 that are disposed between adjacent cylindrical thread elements 12, leaving gaps or lateral openings between adjacent cylindrical thread elements 12. Although the thread elements 12 are illustratively shown in the form of cylinders or rings connected axially-displaced

forming depots 22 include physical or chemical etching techniques. Techniques of laser fabrication or etching to form depots 22 are well-known to one of ordinary skill in the art. Depots 22 can be formed in virtually any stent structure and not merely the above-described structure. The depots 22 are used for carrying a variety of substances including but not limited to therapeutic substances, polymers impregnated with therapeutic substances, radioactive isotopes, and radiopaque materials. The location of a depot 22 or depots 22 vary according to intended usage and application. Depots 22 are formed by a manufacturer at any preselected location and have any preselected depth, size, and geometrical configuration. In one example, depots 22 are evenly distributed through body 16 and have an equal volume so that the tissue in contact with stent 10 receives an equal distribution of a therapeutic substance. Depth D_1 of a depot 22 typically is varied in proportion to the thickness T of body 16 as well as the clinical purpose and usage.

For a stent 10 that carries a therapeutic substance or a polymeric carrier impregnated with a therapeutic substance, a suitable depot or pore depth D_1 has a range from about 10% to about 90 % of thickness T. Typically a depth not greater than about 50% of thickness T is most suitable. The specific depth D_1 of depots 22 depends on the amount of therapeutic substance that is to be deposited in depots 22. In an example of a stent 10 that carries a radioactive isotope, depth D_1 is typically about 10% to about 80% of thickness T. A more specific suitable depth is not greater than about 30% of thickness T is suitable.

For a stent 10 that carries a radiopaque material, a suitable depot or pore depth D_1 has a range from about 10% to about 90% of thickness T. Typically a depth not greater than about 65% is most suitable. A depth D_1 greater than about 65% of the thickness may compromise the structural integrity and mechanical functionality of stent 10. However the upper limit of depth D_1 varies depending on the material characteristics such as the hardness of the body 16.

Depots 22 may be formed in a variety of selected geometrical shapes. Referring to Figure 3A, a depot 22A is a generally cylindrical shape. A diameter D_2 of cylindrical depot 22A typically has a range from about 10% to about 90% of

Porosity determines the capacity of substance that can be loaded into a stent 10 of predetermined dimensions. High porosity can adversely affect the structural integrity, strength, and elasticity of the stent 10. Consequently, stent design includes consideration of a tradeoff between strength, on one hand, and stent profile and stent load capacity on the other hand.

Substances are deposited into the depots or pores 22 using several illustrative methods. The methods are applicable to the illustrative stents 10 described hereinbefore and also to any type of porous prosthesis. In some examples, the deposited substance is a therapeutic substance or agent such as antineoplastics, antiinflammatory substances, antiplatelets, anticoagulants, fribrinolytics, thrombin inhibitors, antimitotics, and antiproliferatives. Examples of antineoplastics include paclitaxel and docetaxel. Examples of antiplatelets, anticoagulants, fribrinolytics, and thrombin inhibitors include sodium heparin, low molecular weight heparin, hirudin, argatroban, forskolin, vapiprost, prostacyclin and prostacyclin analogues, dextran, D-phe-pro-arg-chloromethylketone (synthetic antithrombin), dipyridamole, glycoprotein IIb/IIIa platelet membrane receptor antibody, recombinant hirudin, thrombin inhibitor (available from Biogen), and 7E-3B® (an antiplatelet drug from Centocore). Examples of suitable antimitotic agents include methotrexate, azathioprine, vincristine, vinblastine, flurouracil, adriamycin, and mutamycin. Examples of suitable cytostatic or antiproliferative agents include angiopeptin (a somatostatin analogue from Ibsen), angiotensin converting enzyme inhibitors such as Captopril® (available from Squibb), Cilazapril® (available from Hofman-LaRoche), or Lisinopril® (available from Merck); calcium channel blockers (such as Nifedipine), colchicine, fibroblast growth factor (FGF) antagonists, fish oil (omega 3-fatty acid), histamine antagonist, Lovastatin® (an inhibitor of HMG-CoA reductase, a cholesterol lowering drug from Merck), monoclonal antibodies (such as PDGF receptors), nitroprusside, phosphodiesterase inhibitors, prostaglandin inhibitor (available form Glazo), Seramin (a PDGF antagonist), serotonin blockers, steroids, thioprotease inhibitors, triazolopyrimidine (a PDGF antagonist), and nitric oxide. Other therapeutic substances or agents which may be appropriate include alpha-

For example, Figure 4A illustrates a fluid having a high capillary permeation that corresponds to a solvent contact angle Φ_1 less than about 90°. Figure 4B illustrates a fluid having a low capillary permeation that corresponds to a fluid contact angle Φ_2 greater than about 90°. The first solvent can have a viscosity not greater than about ten centipoise. A high capillary permeation and a viscosity not greater than about ten centipoise allows the first solvent to penetrate into the pores of the prosthesis more quickly, eliminating a requirement to apply the first solvent to the prosthesis for a prolonged period of time. The first solvent can be volatile, facilitating evaporation of the first solvent. Useful examples of some first solvent include, but are not limited to, acetone, ethanol, methanol, isopropanol, tetrahydrofuran, and ethyl acetate. The first solvent is applied to a porous prosthesis, for example by immersing or spraying the solvent in procedures that are well-known to one having ordinary skill in the art.

The first solvent is applied for a predetermined period of time, the specific time depending on the capillary permeation and viscosity of the first solvent, the volume of the pores, and the amount of substance to be deposited. Therapeutic parameters such as the concentration of the therapeutic substance in the solvent and dosages depend on the duration of local release, the cumulative amount of release, and desired rate of release. Correlations and interrelations between the therapeutic parameters are well-known to one having ordinary skill in the art and are simply calculated.

After applying the first solvent for a selected duration, the first solvent is removed from the prosthesis. In one example, the first solvent is removed by evaporation in ambient pressure, room temperature, and anhydrous atmosphere and/or by exposure to mild heat (e.g., 60° C) under a vacuum condition. The prosthesis typically has a clustered or gross formation of a therapeutic substance gathered on the body surface. The cluster is generally removed by immersing the prosthesis in a second fluid and agitating the prosthesis via mechanical perturbation techniques, such as vortexing or vigorous shaking. The second fluid is a non-solvent so that the therapeutic substance does not significantly dissolve in

penetration of the third fluid in the pores. A useful example of a highly volatile third fluid includes, but is not limited to, Freon (e.g., Xerosolv™).

Once loaded, the therapeutic substance remains in the pores until prosthesis deployment and expansion. The expanded prosthesis engages the wall of the anatomical passageway and the therapeutic substance disseminates from the porous cavities and is absorbed into the tissue of the walls of the passageway that are in contact with the prosthesis.

In some embodiments, a surface of the stent is coated with a therapeutic substance in addition to having a therapeutic substance deposited in the pores. A coating of therapeutic substance on the surface of the prosthesis is formed by adding the therapeutic substance to the third fluid rinse. The therapeutic substance is dispersed through the third fluid to form a true solution with the third solvent, rather than a dispersion of fine particles. The therapeutic substance is a substance that is capable of absorbing or attaching to the prosthesis surface. For example, highly suitable therapeutic substances for a stainless steel prosthesis include taxol and dexamethasone. Suitable substances for a Nitinol™ prosthesis include aspirin and heparin. The therapeutic substance added to the third fluid can be the same substance as the therapeutic substance deposited in the pores or a different substance. Rinsing with the third fluid is optionally prolonged or repeated to increase the thickness of the prosthesis therapeutic substance coating.

In another example, a polymeric coating is formed on the surface of the prosthesis, covering the pores containing deposited therapeutic substance. The polymeric coating forms a membrane that reduces the rate of release of a therapeutic substance from the pores. A polymeric material is added to the third fluid rinse to form a coating made from the polymeric material on the prosthesis surface.

The polymeric material, by example and not limitation, forms about 1% to about 3% by weight of the total weight of the solution. The polymeric material is most suitably bio-compatible, including polymers that are non-toxic, non-

about 1% to about 3% by weight of the total weight of the solution. The therapeutic substance, by example and not limitation, typically makes up about 0.3% to about 1% of the total weight of the solution. Once the third solvent is evaporated, a polymeric coating impregnated with a therapeutic substance remains on the surface, covering the therapeutic substance-filled pores.

In another example, a polymeric material, such as any of the polymeric materials listed herein, is impregnated with a therapeutic substance and deposited into the pores. The polymeric material reduces the rate of release of the therapeutic substance from the pores. The method of application includes adding a therapeutic substance and a polymer to a first fluid or solvent. The therapeutic substance is dispersed throughout the first solvent to dissolve into a true solution, or is saturated or supersaturated with the solvent or suspended in fine particles in the first solvent. The polymeric material is also dispersed throughout the first solvent to form a true solution, or is suspended in fine particles in the first solvent. Saturation or supersaturation of the polymer is less suitable since the viscosity of the first solvent is raised beyond a desired limit.

If the therapeutic substance is suspended in the first solvent, the pore size and the diameter of the opening of the pores are to be sufficiently large in comparison to the size of the particles to facilitate loading and unloading of the stent. In one example, suitable pores have a pore size that is more than ten times the particle size of a suspended therapeutic substance and an opening diameter that is more than five times the diameter of the particle size.

The first solvent is selected from among solvents that are compatible with the polymer and therapeutic substance. A first solvent having a high capillary permeation or a contact angle not higher than about 90° improves performance. The first solvent can have a viscosity not higher than about ten centipoise. The first solvent can be volatile to facilitate evaporation. Useful examples of a first solvent include but are not limited to acetone, ethanol, methanol, isopropanol, tetrahydrofuran, and ethyl acetate. The first solvent is applied to a porous prosthesis, by for example, immersing or spraying. The first solvent is applied for

material characteristics. The rinsing is repeated, if desired, until all traces of therapeutic substance and polymeric material are removed from the stent surface.

In an alternative embodiment, the third fluid is capable of significantly dissolving the therapeutic substance but not the polymeric material. As a result, traces of therapeutic substance are removed from the surface of the prosthesis, leaving a polymeric coating covering the surface of the prosthesis including the pores. The polymeric coating serves as an additional rate-reducing membrane. Useful examples of third fluid include but are not limited to DMSO, water, DMSO in an aqueous solution, and glycerol. The third fluid can be removed from the body of the prosthesis using a technique such as evaporation in ambient pressure, room temperature and anhydrous atmosphere and/or by exposure to mild heat (e.g., 60° C) under vacuum condition. The first, second, third fluids, alone or in conjunction with the polymeric material should not adversely affect the characteristics and composition of the therapeutic substance.

In another example, a polymeric material, such as a material capable of swell-loading or post-loading, can be deposited into the pores. Swell-loading occurs when a polymeric carrier is soaked with a therapeutic substance/solvent solution. The polymer swells, receiving the therapeutic substance in the polymer matrices. Once the solvent is removed, the polymer collapses and is impregnated with the therapeutic substance. Examples of polymeric material that are susceptible to swell-loading include thermoplastic polymers such as polyurethanes, polylactic acid, and polyglycolic acid, and non-thermoplastic polymers such as polyethyleneglycol, polyvinyl alcohol, polyacrylamide, and tecophilic polymers. The method of depositing a polymeric material into the pores is generally similar to the above-described methods with an addition of a curing step for the non-thermoplastic polymers subsequent to the rinsing step. One of ordinary skill in the art of polymer fabrication understands how to cure a non-thermoplastic polymer.

In another example, a radiopaque substance such as gold is deposited into the pores. The process of depositing radioactive isotopes is generally similar to the methods described above with a radiopaque substance dispersed and suspended in

room temperature and anhydrous atmosphere or by exposure to mild heat (e.g., 60° C) under vacuum condition. Sintering of the radiopaque material deposited in the pores is performed to bond particles of the radiopaque material without melting the particles. Appropriate pressure and temperature of radiopaque material sintering is specific to the particular material in a manner well known to one having ordinary skill in the art.

Several examples illustrate various methods for depositing substances such as therapeutic substances on a stent. The examples illustrate but do not limit the possible techniques for depositing substances.

EXAMPLE 1

Trapidil is dissolved in ethanol by conventional methods. Trapidil makes up about 15% by weight of the total weight of the solution. A stent having a porous surface is immersed in the solution for 30 minutes. The stent is removed and mounted on a mandrel at ambient pressure, room temperature, and anhydrous atmosphere for approximately 30 minutes, until the ethanol is evaporated. The stent is submerged in hexane, followed by mechanical perturbation in a vortex apparatus for about 15 seconds. The stent is removed from the non-solvent and rinsed with water for about 5 seconds. The stent is dried at ambient pressure, room temperature, and anhydrous atmosphere.

EXAMPLE 2

Trapidil is dissolved in ethanol by conventional methods. Trapidil makes up about 20% by weight of the total weight of the solution. A stent having a porous surface is immersed in the solution for 20 minutes. The stent is removed and mounted on a mandrel at ambient pressure, room temperature, and anhydrous atmosphere for approximately 30 minutes, until the ethanol is evaporated. The stent is submerged in heptane, followed by mechanical perturbation in vortex apparatus for 45 seconds. The stent is removed from the non-solvent and rinsed with dimethylsulfoxide (DMSO) for about 5 seconds. After rinsing, the mandrel is

of the DMSO is evaporated. A polymeric coating remains on the surface of the stent.

EXAMPLE 5

Trapidil is dissolved in ethanol by conventional methods. Trapidil makes up about 20% by weight of the total weight of the solution. A stent having a porous surface is immersed in the solution for 40 minutes. The stent is removed and mounted on a mandrel at ambient pressure, room temperature, and anhydrous conditions for approximately 30 minutes, until the ethanol is evaporated. The stent is submerged in heptane, followed by mechanical perturbation in a vortex apparatus for about 30 seconds. The stent is removed from the non-solvent and rinsed, for about 10 seconds, with a solution containing ethylene vinyl alcohol, trapidil, and DMSO. The ethylene vinyl alcohol constitutes about 1% by weight and the trapidil constitutes about 0.33% by weight of the total weight of the solution. The mandrel is placed in ambient pressure, room temperature, and anhydrous condition for approximately 2 hours. The stent is placed in a oven under vacuum condition and at a temperature of about 60° C for 24 hours, until all of the DMSO is evaporated. A polymeric coating having a trapidil impregnated therein remains on the stent.

EXAMPLE 6

Trapidil was dissolved in ethanol by conventional methods. Trapidil was used to make 40% by weight of the total weight of the solution. A stent having a porous surface was mounted on a mandrel and dipped in the 40% solution for 40 seconds. The stent was removed from the other end and dried at ambient pressure, room temperature, and anhydrous conditions for about 30 minutes, until the ethanol was evaporated. The stent was mounted on a mandrel again and rinsed in a heparin (DuraFlo™)/ Trapidil solution for 3 seconds. The solution constituted 0.6% by weight of Heparin and 0.6% by weight of Trapidil. The solvent used was Freon (Xerosolv) and n-Propanol in the ratio of 5:1 by volume. The stent was placed in a humidity controlled chamber at room temperature for 12 hours until all

CLAIMS

What is claimed is:

1. A method according to loading a substance into pores of an implantable prosthesis:

providing a prosthesis having a surface and pores formed in said surface;

applying a first fluid having an added substance to said prosthesis, wherein during said act of applying, said first fluid penetrates into said pores;

removing said first fluid from said prosthesis substantially to elimination;

applying a second fluid to said prosthesis, wherein during said act of applying said second fluid, said second fluid does not significantly penetrate into said pores; and

removing said second fluid from said prosthesis substantially to elimination, wherein said substance is deposited into said pores.

2. The method according to Claim 1, wherein said acts of removing said first fluid and said second fluid comprise evaporating said first fluid and said second fluid from said prosthesis.

3. The method according to Claim 1, additionally comprising prior to said act of applying said second fluid:

immersing said prosthesis in a third fluid, wherein said substance does not significantly dissolve in said third fluid;

agitating said prosthesis in said third fluid to significantly remove said substance from said surface of said prosthesis, wherein said substance remains in said pores; and

removing said prosthesis from said third fluid.

13. The method according to Claim 7, wherein said second fluid comprises a second therapeutic substance added thereto, such that after said act of significantly removing said second fluid from said prosthesis, a coating of said second therapeutic substance remains on said surface of said prosthesis.

14. The method according to Claim 13, wherein said second therapeutic substance is the same as the first therapeutic substance.

15. The method according to Claim 13, wherein said second therapeutic substance is different than said first therapeutic substance.

16. The method according to Claim 7, wherein said second fluid comprises a polymeric material added thereto, such that after said act of significantly removing said second fluid from said prosthesis, a coating of said polymeric material remains on said surface of said prosthesis.

17. The method according to Claim 7, wherein said second fluid comprises a combination of a polymeric material and a second therapeutic substance added thereto, such that after said act of significantly removing said second fluid from said prosthesis, a coating of said polymeric material containing said second therapeutic substance remains of said surface of said prosthesis.

18. The method according to Claim 1, wherein said substance is a polymeric material.

19. The method according to Claim 18, wherein said polymeric material significantly dissolves when in contact with said second fluid.

20. The method according to Claim 18, wherein said second fluid has a contact angle greater than about 90°.

27. The method according to Claim 24, wherein said polymeric material and said therapeutic substance dissolves when in contact with said second fluid such that any of said polymeric material and said therapeutic substance disposed on said surface of said prosthesis are significantly removed.

28. The method according to Claim 24, wherein said therapeutic substance dissolves when in contact with said second fluid, wherein after said act of significantly removing said second fluid a coating made from said polymeric material remains on said surface of said prosthesis and covers said pores.

29. The method according to Claim 24, wherein said second fluid has a contact angle greater than about 90°.

30. The method according to Claim 1, wherein said substance is a radioactive isotope.

31. The method according to Claim 30, wherein said second fluid has a contact angle greater than about 90°.

32. The method according to Claim 30, additionally comprising prior to said act of applying said second fluid:

immersing said prosthesis in a third fluid;

agitating said prosthesis in said third fluid to significantly remove said radioactive isotope from said surface of said prosthesis; and

removing said prosthesis from said third fluid.

33. The method according to Claim 32, wherein said third fluid has a contact angle greater than about 90°.

34. The method according to Claim 1, wherein said substance is a radiopaque material.

40. The method according to Claim 39, wherein said first fluid has a contact angle less than about 90°.

41. The method according to Claim 39, wherein during said acts of immersing and agitating said second fluid is not capable of significantly penetrate into said pores.

42. The method according to Claim 39, wherein said second fluid has a lower capillary permeation than said first fluid.

43. The method according to Claim 39, wherein said second fluid has a contact angle greater than about 90°.

44. The method according to Claim 39, wherein said substance dissolves when in contact with said third fluid.

45. The method according to Claim 39, wherein said third fluid has a lower capillary permeation than said first fluid.

46. The method according to Claim 39, wherein said third fluid has a contact angle greater than about 90°.

47. An implantable prosthesis, comprising:

a body structure having a generally cylindrical shape, an outer surface capable of contacting an inner lumen surface of a passageway, and a hollow bore which extends longitudinally through said body structure to define an inner surface, said body structure having a thickness;

said body structure having a plurality of depots formed therein, said depots having a depth less than said thickness of said body structure, and said depots having a preselected and controlled distribution and a preselected and controlled depth.

58. The implantable prosthesis of Claim 47 further comprising a therapeutic substance deposited into said depots, wherein said therapeutic substance is selected from a group of antineoplastic, antiplatelet, anticoagulant, fribrinolytics, antimitotic, thrombin inhibitor, antiinflammatory, and antiproliferative substances.

59. The implantable prosthesis of Claim 47 further comprising a therapeutic substance deposited into said depots, wherein said therapeutic substance is a radioactive isotope.

60. The implantable prosthesis of Claim 47 further comprising a substance deposited into said depots, wherein said substance is a polymeric material.

61. The implantable prosthesis of Claim 47 further comprising a substance deposited into said depots, wherein said substance is a polymeric material containing a therapeutic substance.

62. The implantable prosthesis of Claim 47 further comprising a substance deposited into said depots, wherein said substance is a polymeric material containing a therapeutic substance, said therapeutic substance is selected from a group of antineoplastic, antiplatelet, anticoagulant, fibrinolytic, antimitotic, thrombin inhibitor, antiinflammatory, and antiproliferative substances.

63. The implantable prosthesis of Claim 47 further comprising a substance deposited into said depots, wherein said substance is a radiopaque substance.

64. The implantable prosthesis of Claim 47 further comprising a first therapeutic substance deposited in said depots and a polymeric coating formed on said lumen contacting surface of said body, wherein said polymeric coating covers said depots and reduces the rate at which said first therapeutic substance is released from said depots.

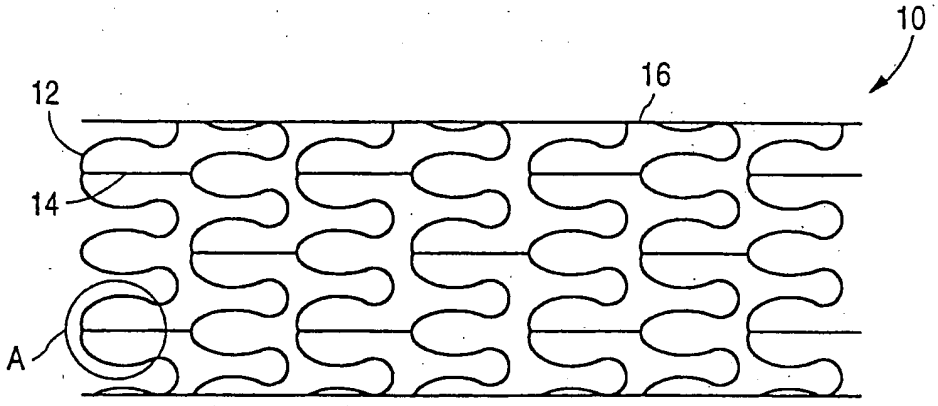

Fig. 1

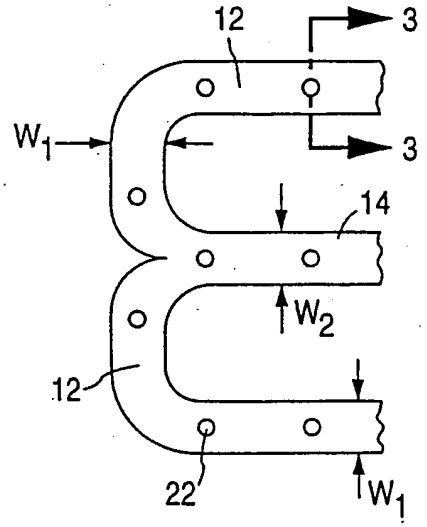

Fig. 2

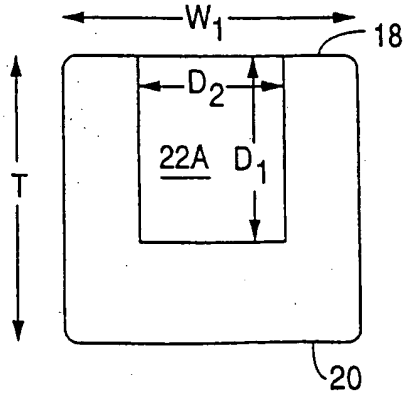

Fig. 3A

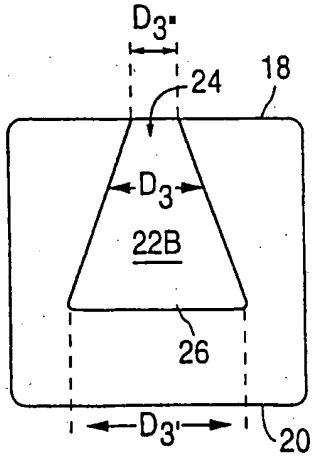

Fig. 3B

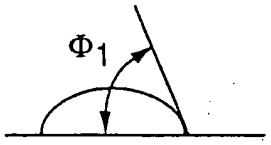

Fig. 4A

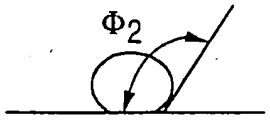

Fig. 4B

INTERNATIONAL SEARCH REPORT

Inten nal Application No
PCT/US 00/23535

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 875 218 A (ADVANCED CARDIOVASCULAR SYSTEM) 4 November 1998 (1998-11-04) column 5, line 19 - line 50 column 6, line 45 - line 55 column 11, line 10 -column 12, line 25	1,7, 16-20, 23,24, 27-29, 47,60-65
A	EP 0 850 651 A (SCHNEIDER USA INC) 1 July 1998 (1998-07-01) abstract column 1, line 42 -column 2, line 20 column 2, line 45 -column 3, line 16 claims 1-10	1,3,4,7, 11,12, 16-22, 25,26, 30,32, 34,37-46
P,X	PATENT ABSTRACTS OF JAPAN vol. 2000, no. 02, 29 February 2000 (2000-02-29) & JP 11 299901 A (JOHNSON &JOHNSON MEDICAL KK), 2 November 1999 (1999-11-02) abstract	47-63

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